

REPLACED BY
ART 34 AMDT

10/539856

What is claimed is:

1. A composition comprising a cyclooxygenase-2 inhibitor or a pharmaceutically acceptable salt of a cyclooxygenase-2 inhibitor and a topoisomerase II inhibitor or a pharmaceutically acceptable salt of a topoisomerase II inhibitor, wherein the cyclooxygenase-2 inhibitor or pharmaceutically acceptable salt of the cyclooxygenase-2 inhibitor is not a 2,3-substituted indole compound or a tetracyclic sulfonylbenzene compound.
2. A composition comprising:
 - a cyclooxygenase-2 inhibitor selected from the group consisting of celecoxib, deracoxib, valdecoxib, rofecoxib, etoricoxib, meloxicam, parecoxib, 4-(4-cyclohexyl-2-methyloxazol-5-yl)-2-fluorobenzenesulfonamide, 2-(3,5-difluorophenyl)-3-(4-(methylsulfonyl)phenyl)-2-cyclopenten-1-one, N-[2-(cyclohexyloxy)-4-nitrophenyl]methanesulfonamide, 2-(3,4-difluorophenyl)-4-(3-hydroxy-3-methylbutoxy)-5-[4-(methylsulfonyl)phenyl]-3(2H)-pyridazinone, 2-[(2,4-dichloro-6-methylphenyl)amino]-5-ethyl-benzeneacetic acid, and (3Z)-3-[(4-chlorophenyl)[4-(methylsulfonyl)phenyl]methylene]dihydro-2(3H)-furanone; and
 - a topoisomerase II inhibitor selected from the group consisting of aclarubicin, amonafide, amrubicin, amsacrine, annamycin, 6,9-bis[(2-aminoethyl)amino]-benz[g]isoquinoline-5,10-dione, 1,11-dichloro-6-[2-(diethylamino)ethyl]-12,13-dihydro-12-(4-O-methyl- β -D-glucopyranosyl)-5H-indolo[2,3-a]pyrrolo[3,4-c]carbazole-5,7(6H)-dione, crisnatol, daunorubicin, doxorubicin, epirubicin, etoposide, galarubicin, idarubicin, iododoxorubicin, 10-[[6-deoxy-2-O-(6-deoxy-3-O-methyl- α -D-galactopyranosyl)-3,4-O-[(S)-phenylmethylene]- β -D-galactopyranosyl]oxy]-5,12-dihydro-1-methyl-5,12-dioxobenzo[h][1]benzopyrano[5,4,3-cde][1]benzopyran-6-yl ester-3-ethoxy-propanoic acid, 8-ethyl-7,8,9,10-tetrahydro-

25 1,6,7,8,11-pentahydroxy-10-[[2,3,6-trideoxy-3-(4-morpholinyl)-
α-L-lyxo-hexopyranosyl]oxy]-5,12-naphthacenedione, (7S,9S)-7-
[[4-O-(3-amino-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl)-2,6-
dideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-
6,9,11-trihydroxy-9-(hydroxyacetyl)-5,12-naphthacenedione,
30 merbarone, mitoxantrone, nemorubicin, pirarubicin, N-[2-
(dimethylamino)ethyl]-9-hydroxy-5,6-dimethyl-6H-pyrido[4,3-
b]carbazole-1-carboxamide, sobuzoxane, teniposide, and
valrubicin.

3. The composition of claim 1 or 2 wherein the
cyclooxygenase-2 selective inhibitor is selected from the
group consisting of celecoxib, deracoxib, valdecoxib,
rofecoxib, etoricoxib, meloxicam, and parecoxib and the
5 topoisoemerase II inhibitor is selected from the group
consisting of aclarubicin, amonafide, amrubicin, amsacrine,
cristnatol, daunorubicin, doxorubicin, epirubicin, etoposide,
idarubicin, mitoxantrone, nemorubicin, pirarubicin,
sobuzoxane, teniposide, and valrubicin.

4. A composition comprising celecoxib and a
topoisoemerase II inhibitor.

5. The composition of any of claims 1, 2, 3, or 4
wherein the topoisoemerase II inhibitor is epirubicin or
idarubicin.

6. A method for treating a neoplasia or a neoplasia
related disorder in a mammal in need of such treatment, the
method comprising administering to the mammal a
therapeutically effective amount of a cyclooxygenase-2
5 inhibitor or a pharmaceutically acceptable salt of a
cyclooxygenase-2 inhibitor and a therapeutically effective
amount of a topoisoemerase II inhibitor or a pharmaceutically
acceptable salt of a topoisoemerase II inhibitor, wherein the

10 cyclooxygenase-2 inhibitor or pharmaceutically acceptable salt
of the cyclooxygenase-2 inhibitor is not a 2,3-substituted
indole compound or a tetracyclic sulfonylbenzene compound.

7. A method for treating a neoplasia or a neoplasia
related disorder in a mammal in need of such treatment, the
method comprising administering to the mammal a
therapeutically effective amount of a cyclooxygenase-2
5 inhibitor selected from the group consisting of celecoxib,
deracoxib, valdecoxib, rofecoxib, etoricoxib, meloxicam,
parecoxib, 4-(4-cyclohexyl-2-methyloxazol-5-yl)-2-
fluorobenzenesulfonamide, 2-(3,5-difluorophenyl)-3-(4-
(methylsulfonyl)phenyl)-2-cyclopenten-1-one, N-[2-
10 (cyclohexyloxy)-4-nitrophenyl]methanesulfonamide, 2-(3,4-
difluorophenyl)-4-(3-hydroxy-3-methylbutoxy)-5-[4-
(methylsulfonyl)phenyl]-3(2H)-pyridazinone, 2-[(2,4-dichloro-
6-methylphenyl)amino]-5-ethyl-benzeneacetic acid, and (3Z)-3-
[(4-chlorophenyl)[4-(methylsulfonyl)phenyl]methylene]dihydro-
15 2(3H)-furanone; and
a topoisomerase II inhibitor selected from the group
consisting of aclarubicin, amonafide, amrubicin, amsacrine,
annamycin, 6,9-bis[(2-aminoethyl)amino]-benz[g]isoquinoline-
5,10-dione, 1,11-dichloro-6-[2-(diethylamino)ethyl]-12,13-
20 dihydro-12-(4-O-methyl- β -D-glucopyranosyl)-5H-indolo[2,3-
a]pyrrolo[3,4-c]carbazole-5,7(6H)-dione, crisnatol,
daunorubicin, doxorubicin, epirubicin, etoposide, galarubicin,
idarubicin, iododoxorubicin, 10-[[6-deoxy-2-O-(6-deoxy-3-O-
methyl- α -D-galactopyranosyl)-3,4-O-[(S)-phenylmethylene]- β -D-
25 galactopyranosyl]oxy]-5,12-dihydro-1-methyl-5,12-
dioxobenzo[h][1]benzopyrano[5,4,3-cde][1]benzopyran-6-yl
ester-3-ethoxy-propanoic acid, 8-ethyl-7,8,9,10-tetrahydro-
1,6,7,8,11-pentahydroxy-10-[[2,3,6-trideoxy-3-(4-morpholinyl)-
 α -L-lyxo-hexopyranosyl]oxy]-5,12-naphthacenedione, (7S,9S)-7-
30 [[4-O-(3-amino-2,3,6-trideoxy- α -L-lyxo-hexopyranosyl)-2,6-

dideoxy- α -L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,9,11-trihydroxy-9-(hydroxyacetyl)-5,12-naphthacenedione, merbarone, mitoxantrone, nemorubicin, pirarubicin, N-[2-(dimethylamino)ethyl]-9-hydroxy-5,6-dimethyl-6H-pyrido[4,3-b]carbazole-1-carboxamide, sobuzoxane, teniposide, and valrubicin.

8. The method of claim 6 or 7 wherein the cyclooxygenase-2 selective inhibitor is selected from the group consisting of celecoxib, deracoxib, valdecoxib, rofecoxib, etoricoxib, meloxicam, and parecoxib and the
5 topoisomerase II inhibitor is selected from the group consisting of aclarubicin, amonafide, amrubicin, amsacrine, cristnatol, daunorubicin, doxorubicin, epirubicin, etoposide, idarubicin, mitoxantrone, nemorubicin, pirarubicin, sobuzoxane, teniposide, and valrubicin.

9. A method for treating a neoplasia or a neoplasia related disorder in a mammal in need of such treatment, the method comprising administering to the mammal a therapeutically effective amount of celecoxib and a
5 topoisomerase II inhibitor.

10. The method of any of claims 6, 7, 8, or 9 wherein the topoisomerase II inhibitor is epirubicin or idarubicin.

11. The method of any of claims 6, 7, 8, 9, or 10 wherein the neoplasia or neoplasia related disorder is selected from the group consisting of a malignant tumor growth selected from the group consisting of acral lentiginous
5 melanoma, actinic keratoses, acute lymphocytic leukemia, acute myeloid leukemia, adenocarcinoma, adenoid cystic carcinoma, adenomas, adenosarcoma, adenosquamous carcinoma, anal canal cancer, anal cancer, anorectum cancer, astrocytic tumors, bartholin gland carcinoma, basal cell carcinoma, biliary
10 cancer, bone cancer, bone marrow cancer, brain cancer, breast

cancer, bronchial cancer, bronchial gland carcinomas,
carcinoids, carcinoma, carcinosarcoma, cholangiocarcinoma,
chondrosarcoma, choroid plexus papilloma/carcinoma, chronic
lymphocytic leukemia, chronic myeloid leukemia, clear cell
15 carcinoma, colon cancer, colorectal cancer, connective tissue
cancer, cystadenoma, digestive system cancer, duodenum cancer,
endocrine system cancer, endodermal sinus tumor, endometrial
hyperplasia, endometrial stromal sarcoma, endometrioid
adenocarcinoma, endothelial cell cancer, ependymal cancer,
20 epithelial cell cancer, esophageal cancer, Ewing's sarcoma,
eye and orbit cancer, female genital cancer, focal nodular
hyperplasia, gallbladder cancer, gastric antrum cancer,
gastric fundus cancer, gastrinoma, germ cell tumors,
glioblastoma, glucagonoma, heart cancer, hemangioblastomas,
25 hemangioendothelioma, hemangiomas, hepatic adenoma, hepatic
adenomatosis, hepatobiliary cancer, hepatocellular carcinoma,
Hodgkin's disease, ileum cancer, insulinoma, intraepithelial
neoplasia, interepithelial squamous cell neoplasia,
intrahepatic bile duct cancer, invasive squamous cell
30 carcinoma, jejunum cancer, joint cancer, Kaposi's sarcoma,
kidney and renal pelvic cancer, large cell carcinoma, large
intestine cancer, larynx cancer, leiomyosarcoma, lentigo
maligna melanomas, leukemia, liver cancer, lung cancer,
lymphoma, male genital cancer, malignant melanoma, malignant
35 mesothelial tumors, medulloblastoma, medulloepithelioma,
melanoma, meningeal cancer, mesothelial cancer, metastatic
carcinoma, mouth cancer, mucoepidermoid carcinoma, multiple
myeloma, muscle cancer, nasal tract cancer, nervous system
cancer, neuroblastoma, neuroepithelial adenocarcinoma nodular
40 melanoma, non-epithelial skin cancer, non-Hodgkin's lymphoma,
oat cell carcinoma, oligodendroglial cancer, oral cavity
cancer, osteosarcoma, ovarian cancer, pancreatic cancer,
papillary serous adenocarcinoma, penile cancer, pharynx
cancer, pituitary tumors, plasmacytoma, prostate cancer,

45 pseudosarcoma, pulmonary blastoma, rectal cancer, renal cell
carcinoma, respiratory system cancer, retinoblastoma,
rhabdomyosarcoma, sarcoma, serous carcinoma, sinus cancer,
skin cancer, small cell carcinoma, small intestine cancer,
smooth muscle cancer, soft tissue cancer, somatostatin-
50 secreting tumor, spine cancer, squamous cell carcinoma,
stomach cancer, striated muscle cancer, submesothelial cancer,
superficial spreading melanoma, T cell leukemia, testicular
cancer, thyroid cancer, tongue cancer, undifferentiated
carcinoma, ureter cancer, urethra cancer, urinary bladder
55 cancer, urinary system cancer, uterine cervix cancer, uterine
corpus cancer, uveal melanoma, vaginal cancer, verrucous
carcinoma, VIPoma, vulva cancer, well differentiated
carcinoma, and Wilms tumor.

12. The method of any of claims 6, 7, 8, 9, or 10
wherein the neoplasia or neoplasia related disorder is
selected from the group consisting of lung cancer, colorectal
cancer, breast cancer, prostate cancer, bladder cancer, ovary
5 cancer, cervical cancer, gastrointestinal cancer, and
leukemia.

13. The method of any of claims 6, 7, 8, 9, or 10
wherein the neoplasia or neoplasia related disorder is
selected from the group consisting of lung cancer, colorectal
cancer, breast cancer, prostate cancer, bladder cancer, ovary
5 cancer, and central nervous system cancer.